

said residues being protonated in a weak acid medium, said protonation leading to a destabilization of a cellular membrane,

b) said protonable residues possess the following properties:

said protonable residues contain a functional group enabling them to be linked to said oligomer,

said protonable residues are not recognized as a recognition signal by a cellular membrane receptor,

C, said protonable residues comprise at least one free NH_3^+ group,

c) the free NH_3^+ of said monomers can be also substituted by uncharged residues leading to a reduction of the number of positive charges in comparison to the same oligomer before substitution,

d) molecules constituting a recognition signal recognized by a membrane cellular receptor may be present:

by substitution of some of the free NH_3^+ of said monomers,

on some of the uncharged residues leading to a reduction of the number of charges,

on some of said protonable residues leading to a destabilization of a cellular membrane, or

by substitution of the free NH_3^+ (if it is present) of said protonable residues leading to a destabilization of a cellular membrane, provided that:

1) the total number of the non-substituted NH_3^+ functions is of at least 50 % of the polymerization degree,

2) the number of monomers initially carrying free NH_3^+ is substituted in a ratio of at least 50 % of the polymerization degree by residues leading to a destabilization of the cellular membrane.--

--2. (amended) The oligomeric conjugate according to claim 1, wherein the protonable residues leading to a destabilization of cellular membranes wherein said protonable residues have a pK in aqueous medium lower than 8.0.--

--3. (amended) The oligomeric conjugate complex according to claim 1, wherein said protonable residues are compounds selected from the group consisting of:

imidazoles,
quinolines,
pterines, and
pyridines.--

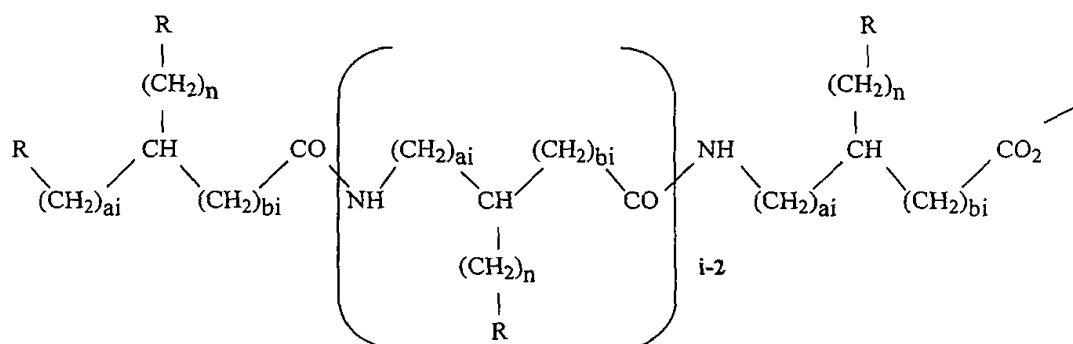
--4. (amended) The oligomeric conjugate according to claim 1, wherein said protonable residues comprise

alkylimidazoles in which the alkyl radical has from 1 to 10 carbon atoms, and only one nitrogen atom of the imidazole ring is substituted.--

C
--5. (amended) The oligomeric conjugate according to claim 1, wherein the protonable residues leading to a destabilization of cellular membranes are selected from the group consisting of

histidine, 4-carboxymethyl-imidazole,
3-(1-methyl-imidazol-4yl)-alanine, 3-(3-methyl-imidazol-4yl)-alanine,
2-carboxy-imidazole, histamine, 3-(imidazol-4yl)-L-lactic acid,
2-(1-methyl-imidazol-4yl)ethylamine, 2-(3-methyl-imidazol-4yl)ethylamine,
β-alanyl-histidine-(carnosine), 7-chloro-4(amino-1-methylbutylamino)-quinoline,
N4-(7-chloro-4-quinolinyl)-1,4-pentanediamine,
8-(4-amino-1-methylbutylamino)-6-methoxy-quinoline (primaquine),
N4-(6-methoxy-8-quinolinyl)1,4-pentanediamine, quininic acid,
quinoline carboxylic acid, pteronic acid, nicotinic acid, and quinolinic acid.--

--6. (amended) The oligomeric conjugate according to claim 1, wherein the oligomeric conjugate contains an oligomer of the following formula:



Wherein:

ai is an integer varying from 0 to 10,

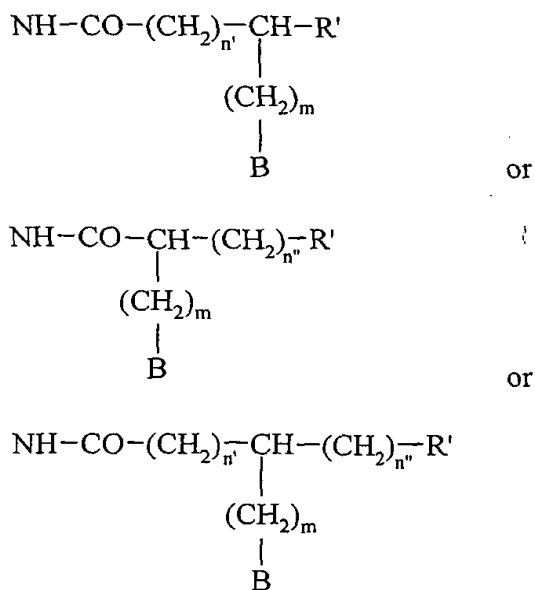
bi is an integer varying from 0 to 10,

i = degree of polymerization from 5 to

36,

n = is an integer varying from 1 to 6,

R represents in a ratio of 50 % to 100 %
(corresponding to a number u)



m is an integer varying from 1 to 6,

n' is an integer varying from 0 to 6,

n" is an integer varying from 0 to 6,

B is a weak base,

R' represents NH_3^+ (corresponding to a number p),
or NH (corresponding to a number q) substituted
by

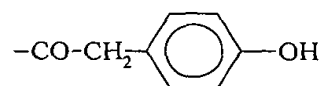
-CO-CH₃

-CO-(CHOH)_rH

r being an integer from 1 to
15, and preferably 1 to 7

-CO-(CH₂)_s-(CHOH)_rH

r being an integer from
1 to 15, and s being an
integer from 1 to 6,



-SO₂-Flu

-CO-Flu

-CS-NH-Flu

Flu being a fluorescent molecule

* R represents in a ratio of 0 % to 50 %
(corresponding to f: $0 < f \leq u$)

NH_3^+ (corresponding to a number j),

NH (corresponding to a number k), substituted
by

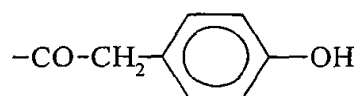
-CO-CH₃

-CO-(CHOH)_rH

r being an integer from
1 to 15,

-CO-(CH₂)_s-(CHOH)_rH

r being an integer from
1 to 15, and s being an
integer from 1 to 6,



-SO₂-Flu

-CO-Flu

-CS-NH-Flu

Flu being a fluorescent molecule

H (corresponding to a number h)

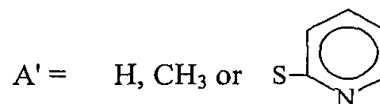
(CH₂)_nH, n being an integer from
1 to 6

(corresponding to a number h)

(CH₂)_n-OH n being an integer from
1 to 6

(corresponding to a number h)

(CH₂)_n-SA'



(corresponding to a number h) n being an integer from
1 to 6

with i = u + j + k + h

total number of α NH₃⁺ = p = u - q

total number of ω NH₃⁺ = j = f - (k + h)

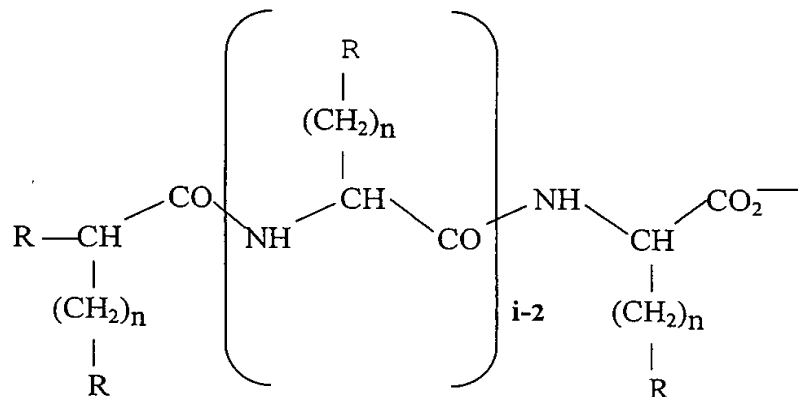
total number of NH₃⁺ = m = pⁱ + j + 1

with the proviso that:

1) u ≥ i/2

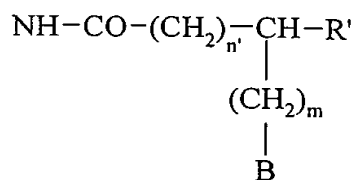
2) m ≥ i/2

--7. (amended) The oligomeric conjugate according to claim 1, wherein the oligomeric conjugate contains an oligomer of the following formula:

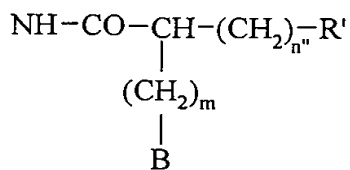


wherein

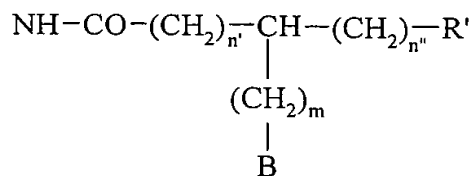
- * i = degree of polymerization from 5 to 36,
- * n = is an integer varying from 1 to 6,
- * R represents in a ratio of 50 % to 100 % (corresponding to u)



or



or



m is an integer varying from 1 to 6,

n' is an integer varying from 0 to 6,

n'' is an integer varying from 0 to 6,

B is a weak base,

R' represents NH_3^+ (corresponding to a number p),
or NH (corresponding to a number q) substituted by

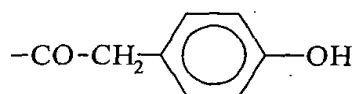
-CO-CH₃

-CO-(CHOH)_rH

r being an integer from 1
to 15,

-CO-(CH₂)_s-(CHOH)_rH

r being an integer from
1 to 15, and s being an
integer from 1 to 6,



-SO₂-Flu

-CO-Flu

-CS-NH-Flu

Flu being a fluorescent molecule

* R represents in a ratio of 0 % to 50 %
(corresponding to f: $0 < f \leq 1$)

NH_3^+ (corresponding to a number j),

NH (corresponding to a number k), substituted by

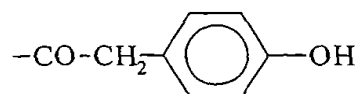
-CO-CH₃

-CO-(CHOH)_rH

r being an integer from 1
to 15,

-CO-(CH₂)_s-(CHOH)_rH

r being an integer from 1
to 15, and s being an
integer from 1 to 6



-SO₂-Flu

-CO-Flu

-CS-NH-Flu

Flu being a fluorescent molecule

H (corresponding to a number h)

$(CH_2)_nH$, n being an integer from
1 to 6

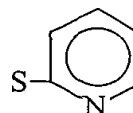
(corresponding to a number h)

$(CH_2)_n-OH$ n being an integer from
1 to 6

(corresponding to a number h)

$(CH_2)_n-SA'$

A' = H, CH₃ or S-



(corresponding to a number h)

n being an integer from
1 to 6

with $i = u + j + k + h$

total number of $\alpha NH_3^+ = p = u - q$

total number of $\omega NH_3^+ = j = f - (k + h)$

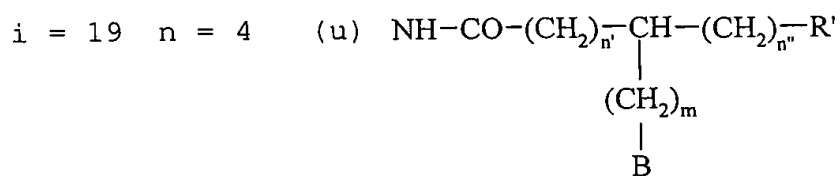
total number of $NH_3^+ = m = p + j + 1$

with the proviso that :

1) $u \geq i/2$

2) $m \geq i/2$

--8. (amended) The oligomeric conjugate according to
claim 7, wherein:



wherein

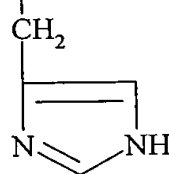
$$n' = n'' = 0$$

$$\text{R}' = \text{NH}_3^+$$

$$m = 1$$

$$\text{B} = \text{imidazole}$$

$$\text{R} = \text{NH}-\text{CO}-\text{CH}-\text{NH}_3^+$$

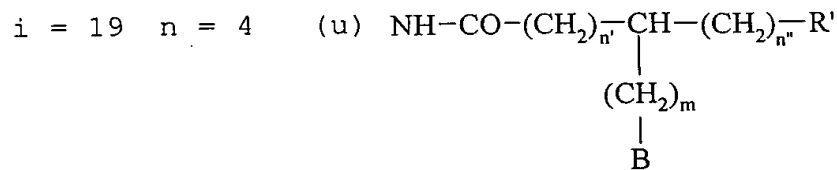


(f) $\text{R} = \text{NH}_3^+$

$$u = 12$$

$$j = 7$$

or



wherein

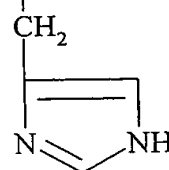
$$n' = n'' = 0$$

$$\text{R}' = \text{NH}_3^+$$

$$m = 1$$

$$\text{B} = \text{imidazole}$$

$$\text{R} = \text{NH}-\text{CO}-\text{CH}-\text{NH}_3^+$$

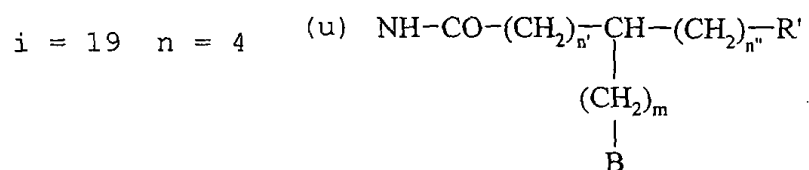


(f) $\text{R} = \text{NH}_3^+$

$$u = 16$$

$$j = 3$$

or



wherein

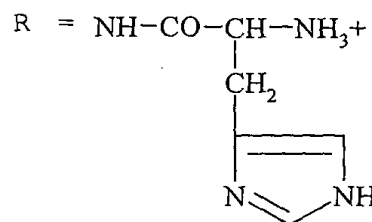
$$n' = n'' = 0$$

$$\text{R}' = \text{NH}_3^+$$

$$m = 1$$

$$\text{B} = \text{imidazole}$$

C

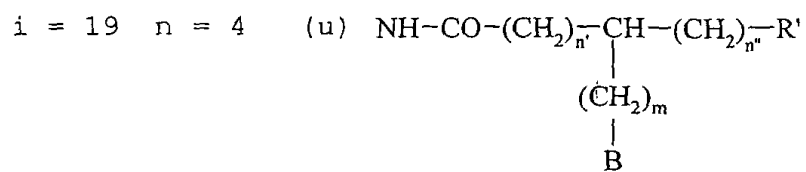


$$(f) \quad \text{R} = \text{NH}_3^+$$

$$u = 19$$

$$j = 0$$

or



wherein

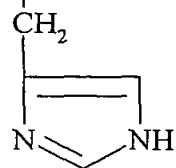
$$n' = n'' = 0$$

$$R' = \text{NH}_3^+$$

$$m = 1$$

$$B = \text{imidazole}$$

$$R = \text{NH-CO-CH-NH}_3^+$$



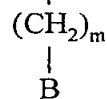
$$(f) R = \text{CO-CH}_3$$

$$u = 11$$

$$k = 8$$

or

$$i = 19 \quad n = 4 \quad (u) \quad \text{NH-CO-(CH}_2\text{)}_n\text{-CH-(CH}_2\text{)}_{n''}\text{-R'}$$



wherein

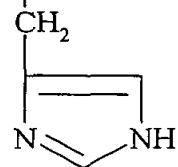
$$n' = n'' = 0$$

$$R' = \text{NH}_3^+$$

$$m = 1$$

$$B = \text{imidazole}$$

$$R = \text{NH-CO-CH-NH}_3^+$$

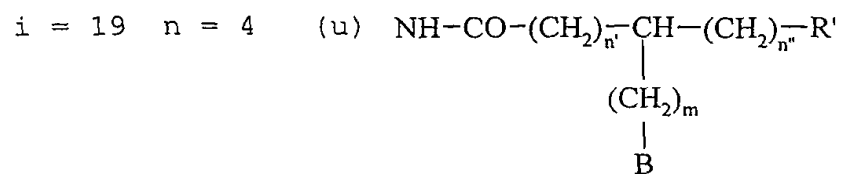


$$(f) R = \text{CO-CH}_3$$

$$u = 15$$

$$k = 4$$

or



wherein

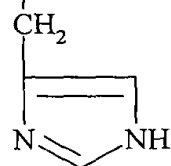
$$n' = n'' = 0$$

$$\text{R}' = \text{NH}_3^+$$

$$m = 1$$

$$\text{B} = \text{imidazole}$$

$$\text{R} = \text{NH-CO-CH-NH}_3^+$$



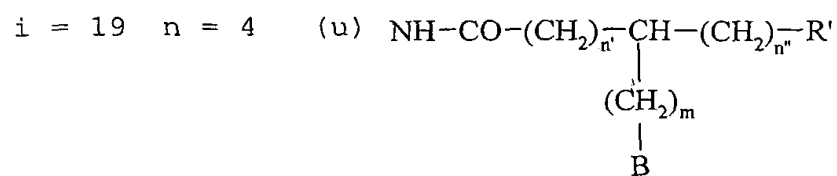
$$(f) \quad \text{R} = \text{CO-(CHOH)}_r\text{H}$$

$$r = 5$$

$$u = 12$$

$$k = 3$$

or



wherein

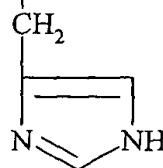
(q) $n' = n'' = 0$

$R' = \text{NH-CO-CH}_3$

$m = 1$

$B = \text{imidazole}$

$R = \text{NH-CO-CH-NH}_3^+$



(f) $R = \text{NH}_3^+$

$u = 16$

$f = 4$

$k = 3$

--9. (amended) A composition comprising an oligomeric conjugate according to claim 8, in association with at least one biological molecule, selected from the group consisting of a peptide, an oligoside, an oligonucleotide, and a mixture thereof.

--10. (amended) A combined preparation, in the form of a kit-of-parts, comprising:

- a) an oligomeric conjugate according to claim 1, and
- b) a biological molecule, selected from the group consisting of a peptide, an oligoside, an oligonucleotide, and a mixture thereof,

for the simultaneous, separate or sequential use, for the *in vitro*, *in vivo*, or *ex vivo* transfer of said biological molecules into a cytosol and/or cell nucleus.--

--11. (amended) A method for the *in vitro*, *ex vivo*, or *in vivo* intracellular transfer of biological molecules into a cytosol and/or in a cell nucleus of a cell, comprising:

treating said cell with an oligomeric conjugate according to claim 1 in association with a biological material.--

C' --12. (amended) A method for the *in vitro*, *ex vivo*, or *in vivo* transfer of a peptide, an oligoside or an oligonucleotide, or a mixture thereof, into a cytosol and/or a cell nucleus of a cell, comprising:

treating said cell with an oligomeric conjugate according to claim 1 in association with said peptide, oligoside, oligonucleotide and mixture thereof.--

--13. (amended) The method according to claim 11, wherein the cells are selected from the group consisting of muscular, epithelial, endothelial, and myeloid cells.--

--14. (amended) A method for the *in vivo*, *in vitro* or *ex vivo* transfer of an oligonucleotide, comprising contacting an oligonucleotide and an oligomeric conjugate according to claim 1 with a medium containing cells, wherein:

an antisense oligonucleotide is transferred into a cytosol and/or the cell nucleus where it binds and blocks the complementary mRNA sequence;

an oligonucleotide is transferred into a cytosol where it depresses or activates a messenger in a cytosol, or the corresponding gene in the nucleus;

oligonucleotides corresponding to a repetitive bacterial type DNA sequence with stimulating or immunodepressive activity;

an oligonucleotide is transferred into the cell nucleus where it binds to DNA and forms a triple helix leading to the inhibition of gene expression;

oligonucleotides are transferred into a cytosol and/or cell nucleus which inhibit gene expression by blocking the binding of regulatory factors to the specific DNA region;
or

ribozymes (RNA oligonucleotides) which inhibit gene expression by cleaving the mRNA are transferred into a cytosol, and/or cell nucleus.--

--17. (amended) A pharmaceutical composition, comprising as an active substance, an oligomeric conjugate according to claim 1, in association with a pharmaceutically acceptable vehicle.
